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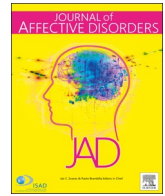
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## Research paper

Associations of depressive symptoms and history with three *a priori* diet quality indices in middle-aged and older adultsLiset E.M. Elstgeest<sup>a,\*</sup>, Laura H.H. Winkens<sup>a</sup>, Brenda W.J.H. Penninx<sup>b</sup>, Ingeborg A. Brouwer<sup>a</sup>, Marjolein Visser<sup>a</sup><sup>a</sup> Department of Health Sciences, Faculty of Science, Amsterdam Public Health research institute, Vrije Universiteit Amsterdam, De Boelelaan 1085, 1081 HV Amsterdam, The Netherlands<sup>b</sup> Department of Psychiatry, Amsterdam Public Health research institute, Amsterdam UMC, Vrije Universiteit Amsterdam, Oldenaller 1, 1081 HJ Amsterdam, The Netherlands

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## ABSTRACT

**Background:** Evidence for the diet-depression link is growing but longitudinal studies on the reverse association are scarce. We investigated associations of (1) current depressive symptoms, (2) short-term changes in and (3) long-term history of depressive symptoms with three *a priori* diet quality indices.**Methods:** Data were from participants ( $\geq 55$  years) of the Longitudinal Aging Study Amsterdam (LASA). The Mediterranean Diet Score (MDS), Alternative Healthy Eating Index (AHEI-2010) and Dietary Approaches to Stop Hypertension diet (DASH) were derived in 2014/2015. Depressive symptoms (Center for Epidemiologic Studies Depression scale; CES-D) were assessed in 2014/2015 and at five regular 3-yearly cycles from 2001–2003 to 2015/2016. Associations between three depression determinants and the diet indices were analysed by multi-variable linear regression models.**Results:** Cross-sectionally ( $n = 1312$ ), current depressive symptoms ( $\text{CES-D} \geq 16$ ) were associated with lower MDS (adjusted  $B = -1.21$ , 95%CI =  $-2.41, -0.023$ ) and AHEI ( $B = -2.72$ , 95%CI =  $-5.24, -0.20$ ) scores in men only. Chronic/recurrent depressive symptoms ( $\text{CES-D} \geq 16$  in both 2011–2013 and 2015/2016) were associated with lower MDS scores ( $n = 1233$ ;  $B = -2.22$ , 95%CI =  $-3.40, -1.04$ ) and a trend for lower AHEI scores ( $B = -2.37$ , 95%CI =  $-4.92, 0.18$ ), compared to no depressive symptoms (twice  $\text{CES-D} < 16$ ). History of depressive symptoms (ever  $\text{CES-D} \geq 16$  from 2001–2003 to 2011–2013;  $n = 687$ ) was associated with lower MDS ( $B = -1.87$ , 95%CI =  $-3.47, -0.27$ ) and AHEI ( $B = -4.33$ , 95%CI =  $-7.54, -1.13$ ) scores in men only. No associations were found with the DASH score.**Limitations:** Single dietary data collection impeded investigation of prospective depression-diet associations.**Conclusions:** Our study in middle-aged and older adults suggests that current and past depressive symptoms are associated with poorer diet quality, particularly in men.

## 1. Introduction

Diet has been investigated in relation to physical health for several decades; however, the role of diet in mental health is an emerging field of research. Diet might be an important, modifiable risk factor for mental illnesses, including depression. Reviews and meta-analyses on dietary patterns and depression concluded that ‘healthy’, ‘traditional’ and ‘Mediterranean’ dietary patterns may play a protective role, while

‘unhealthy’ and ‘Western’ dietary patterns may increase the risk of depression. However, the individual observational studies showed different findings, and evidence for a true causal association is still lacking (Lai et al., 2014; Lassale et al., 2018; Molendijk et al., 2018; Psaltopoulou et al., 2013; Quirk et al., 2013; Rahe et al., 2014). Furthermore, a recent review on late life depression of Gougeon (2016) suggested that the evidence for an association appears less conclusive in older adults. It is also unclear whether the diet-depression link is sex-

**Abbreviations:** AHEI, Alternative Healthy Eating Index 2010; BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression scale; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; FFQ, food frequency questionnaire; HELIUS, Healthy Life in an Urban Setting study; IQR, interquartile range; LASA, Longitudinal Aging Study Amsterdam; MDS, Mediterranean Diet Score; MMSE, Mini-Mental State Examination; RQ, research question; SD, standard deviation

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specific (Akbaraly et al., 2013; Knüppel et al., 2017; Lassale et al., 2018; Le Port et al., 2012; Vermeulen et al., 2018).

Most previous studies investigated the association of dietary patterns with depressive symptoms. However, a poor diet may not be one of the causes of depression but (also) a negative consequence of the disorder. This is known as the ‘reverse causality hypothesis of diet and depression’. Depressive mood and stress can have an impact on food intake via physiological pathways that influence appetite or other behaviours (Adam and Epel, 2007; Gibson, 2006). Stressful events can lead to less healthy food choices, such as higher intake of energy-dense, high-fat foods, and subsequently to obesity (Laitinen et al., 2002; Popa and Ladea, 2012). Previous studies showed that depressive symptoms were associated with poorer overall diet quality (Gibson-Smith et al., 2018), higher intakes of saturated fat, sugar and sodium (Appelhans et al., 2012) and higher sweet foods and lower low-calorie foods consumption (Jeffery et al., 2009). A positive association was also observed with total caloric intake from saturated fat and total sugars (Whitaker et al., 2014). Other studies showed an inverse (Beydoun et al., 2009; Crawford et al., 2011; Pagoto et al., 2009) or no association (Beydoun et al., 2009; Beydoun and Wang, 2010) between depressive symptoms and the likelihood of eating a healthy diet. All eight studies had a cross-sectional design, which does not assure the causality or temporality of associations.

Some prospective studies investigating the influence of diet on depression or depressive symptoms tested the possibility of ‘reverse causality’, whereby depression affects diet. This was conducted – mostly as sensitivity analysis – by excluding participants who reported depressive symptoms at baseline from the analysis or by analysing the reverse association as well. These studies suggested that diet influences depression or depressive symptoms but not vice versa (e.g. Akbaraly et al., 2009, 2013; Chocano-Bedoya et al., 2013; Kingsbury et al., 2016; Knüppel et al., 2017; Rienks et al., 2013; Sánchez-Villegas et al., 2009; Skarupski et al., 2013; Smith et al., 2014; Tsai et al., 2012). However, a recent study in three age cohorts (20+, 40+, 60+ years) showed that reverse causality in the relationship between diet and depression existed, but that the association differed according to the disease status. Current depression was associated with lower scores on the healthy pattern, while past depression led to higher scores on the healthy dietary pattern and lower scores on the western pattern (Jacka et al., 2015). This study had as limitation that history of depression was asked retrospectively. Recently, a nested case-control study investigated whether incidence of depressive symptoms was associated with changes in nutrient intakes during the year ‘depression’ was detected (Gougeon et al., 2017). This study did not show significantly different changes in intakes of energy, fibre, protein and saturated fat between cases (who became depressed) and controls (who remained non-depressed); however, small declines in dietary intake of three B vitamins may have preceded ‘depression’ incidence. This study on the reverse causality hypothesis in older adults did not seem to support this hypothesis; however, the follow-up duration was only one year. More longitudinal studies of longer duration on the relationship from depression to diet are clearly needed.

Therefore, we aimed to study the association between depressive symptoms and three *a priori* diet quality indices: Mediterranean Diet Score (MDS), Alternative Healthy Eating Index (AHEI) and Dietary Approaches to Stop Hypertension diet (DASH). We chose these indices as they all measure a healthy diet and are used worldwide in relation to disease. Furthermore, because they differ in dietary components, it is possible to gain some insight into which food groups may be strongest associated with depression by comparing the indices. Next to the cross-sectional associations (research question 1; RQ1), we also investigated how history of depressive symptoms is associated with adherence to the diet indices. For this longitudinal approach, we studied associations of both short-term changes in depressive symptoms (2 to 5 years) (RQ2) as well as the long-term history of depressive symptoms (2 to 14 years) (RQ3) with the three diet quality indices. In this way, we could

discriminate whether recent mood changes or depressed mood during a longer life period are important determinants of diet quality.

## 2. Methods

### 2.1. Study population

The Longitudinal Aging Study Amsterdam (LASA) is an ongoing cohort study in a nationally representative sample of the Dutch older population aged 55 years and older living in three geographic regions in the Netherlands. Data have been collected to study the determinants, trajectories and consequences of physical, cognitive, emotional and social functioning in relation to aging. Every three years measurement cycles are carried out at the participants’ homes, including a main interview, medical interview and questionnaire. In subpopulations, side studies have been performed. LASA comprises three cohorts: the first cohort (aged 55–85 years at baseline) was recruited at LASA’s start in 1992/1993, the second (55–65 years) in 2002/2003 and the third (55–65 years) in 2012/2013. All participants provided written informed consent, and the Medical Ethics Committee of the VU University Medical Center approved this study and the side studies. A detailed description of the sampling and data collection procedures can be found elsewhere (Hoogendijk et al., 2016; Huisman et al., 2011).

### 2.2. Participants

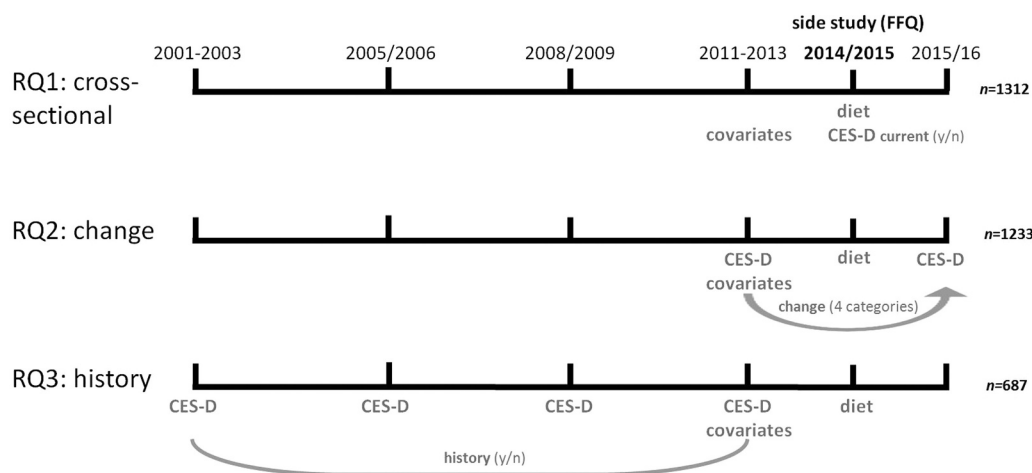
For the present study, we used data of persons participating in the ‘LASA Nutrition and Food-related Behaviour study’: a side study conducted in 2014/2015 that consisted of a questionnaire (paper or online), including a food frequency questionnaire (FFQ) and questions on food-related behaviour and mental well-being. A total of 2089 persons of the three LASA cohorts were approached, of which 1439 persons participated in the side study – see Fig. 1 of Winkens et al., (2018) for a flow chart of this side study. We excluded 32 persons with no or incomplete data on the Center for Epidemiologic Studies Depression scale (CES-D), 7 persons with more than 10 missing values on the FFQ questions, 26 persons with an implausible energy intake (< 800 kCal or > 4000 kCal for men and < 500 kCal or > 3500 kCal for women) (Willett, 1998) and 62 persons with missing data on relevant confounders. This resulted in an analytical sample of 1312 persons for the cross-sectional analyses (RQ1). For the short-term change analyses (RQ2), 79 persons with no or incomplete CES-D data at the measurement cycle before (2011–2013) or after (2015/2016) the side study were additionally excluded, leaving 1233 persons for the analytical sample. For the long-term history analyses (RQ3), cohort 3 ( $n = 604$ ) needed to be excluded from the analytical sample of RQ1 ( $n = 1312$ ) since this cohort just started in 2012/2013, as well as 21 persons with no or incomplete CES-D data at any of the four cycles before the side study (from cycle 2001–2003); this resulted in an analytical sample of 687 persons. Fig. 1 shows the measurement cycles used for the three RQs: from 2001–2003 to 2015/2016.

### 2.3. Dietary assessment

At the side study in 2014/2015, dietary intake was assessed with the Dutch version of the FFQ of the HEalthy Life in an Urban Setting study (HELIUS) (Beukers et al., 2015). This semi-quantitative FFQ consists of 238 food items and asks for consumption during the past 4 weeks. To calculate nutrient intake, each food item was linked to one or more foods of a nutrient database, which was based on the Dutch Food Composition Table (2011).

### 2.4. Diet quality indices

An overview of the scoring criteria of the three diet indices is presented in Table 1. The MDS of Panagiotakos et al. (2007) comprises 11



**Fig. 1.** Schematic overview of measurement cycles used for each research question from the Longitudinal Aging Study Amsterdam.

Abbreviations: CES-D, Center for Epidemiologic Studies Depression scale; FFQ, food frequency questionnaire; RQ, research question.

At the regular cycles, the CES-D was assessed during an interview; at the side study, the CES-D was assessed with a self-reported questionnaire.

components (food groups), each scoring from 0 to 5 based on intake in weekly or daily servings. The AHEI-2010 of [Chiuve et al. \(2012\)](#) is based on foods and nutrients predictive of chronic disease risk and includes 11 components scoring from 0 to 10. The DASH of [Fung et al. \(2008\)](#) scores intake quintiles of 8 components (food groups and nutrient). Both the AHEI-2010 and DASH originally include sodium as one of the components. However, discretionary salt use was not asked in our FFQ, and sodium intake was not calculated from the FFQ items as this is very difficult ([McLean, 2014](#)); thus, our versions of the AHEI and DASH include one component less. For all indices, a higher score indicates adherence to a healthier diet generally associated with a lower chronic disease risk. The food items of the indices' components are shown in **Supplemental Table 1**.

## 2.5. Depressive symptoms measurements

At the side study and each regular measurement cycle, the CES-D was used to measure depressive symptoms during the past week ([Radloff, 1977](#)). This self-report symptom-rating scale consists of 20 items, which are scored on a 4-point scale. The total score ranges from 0 to 60 with a higher score indicating a higher level of depressive symptoms. The CES-D has been used extensively in older population-based samples and is considered a valid and reliable screening instrument for Dutch older adults ([Beekman et al., 1997](#)). At regular cycles, the CES-D was assessed during an interview, while at the side study, the CES-D was assessed using a self-reported questionnaire.

The cutoff score of  $\geq 16$  was used to indicate clinically relevant depressive symptoms; this cutoff has a sensitivity of 100% and a specificity of 88% in the first LASA cohort ([Beekman et al., 1997](#)). For RQ1, the presence of depressive symptoms (yes/no) was used as determinant. For RQ2, short-term changes in depressive symptoms from 2011–2013 to 2015/2016 were divided into four categories: 'no depressive symptoms' (no-no), 'emerging depressive symptoms' (no-yes), 'remitted depressive symptoms' (yes-no) and 'chronic/recurrent depressive symptoms' (yes-yes). In line with [Penninx et al. \(2000\)](#) and [Van Gool et al. \(2003\)](#), a relevant change in depressive mood was defined as an increase (emerging depressive symptoms) or decrease (remitted depressive symptoms) of 4 CES-D points or more between the two measurements, thereby crossing the cutoff score of 16. Persons who did not fulfil the condition of relevant change (4 points) were categorised as 'no depressive symptoms' or 'chronic/recurrent depressive symptoms', depending on their starting level of depressive symptoms. For RQ3, long-term history of depressive symptoms (yes/no) was used as determinant: CES-D score  $< 16$  at all cycles versus CES-D score  $\geq 16$  at any of the four regular cycles before the side study (2001–2003, 2005/2006, 2008/2009 and/or 2011–2013).

## 2.6. Covariates

Data on age and sex were derived from the municipal registries. Marital status was categorised into married/registered partnership, never married and widowed/divorced. The highest completed level of education was divided into low (elementary school or less), middle (general secondary, intermediate vocational, intermediate general and lower vocational education) and high (university education, college or higher vocational). Body mass index (BMI) was calculated by dividing measured body weight (in kg) by the squared measured body height (in m). Waist circumference (in cm) was measured twice and the mean was calculated. Categories of self-reported smoking status were never, former and current smoking. Self-reported alcohol use was categorised into no, light, moderate and (very) excessive ([Garretsen, 1983](#)). Total energy intake was calculated from the FFQ. Physical activity during the past 2 weeks (walking outdoors, cycling, light and heavy household activities and sports, in MET-hours/week) was assessed using the validated LASA Physical Activity Questionnaire ([Stel et al., 2004](#)). Self-reported number of chronic diseases included major somatic diseases: asthma/chronic obstructive pulmonary disease, cardiac disease, peripheral arterial disease, diabetes mellitus, cerebrovascular accident/stroke, osteoarthritis/rheumatoid arthritis, cancer, hypertension and other chronic diseases. General cognitive functioning was measured with the Mini-Mental State Examination (MMSE, only used in sensitivity analyses), which score ranges from 0 to 30 ([Folstein et al., 1975](#)). Use of antidepressants (yes/no, only used in sensitivity analyses) was retrieved during the medical interviews at the regular cycles using ATC-codes of the medications used at that time by the participant. At the side study, a question asked about current use of antidepressants (yes/no). As most covariates were not included in the side study's questionnaire, data on all covariates were measured at the cycle before the side study (2011–2013), with the exception of energy intake and antidepressant use at the side study (2014/2015).

## 2.7. Statistical analyses

Characteristics were described as means and standard deviations (SD) or medians and interquartile ranges (IQR), and as percentages. Intakes of the diet quality indices' components were described as medians and IQRs.

The MDS, AHEI and DASH outcomes were checked by analysis of residuals and appeared normally distributed; therefore, they were analysed as continuous outcomes. Multivariable linear regression models were used to analyse the associations of all three RQs, i.e. the associations between the specific depression determinant and the diet indices ([Fig. 1](#)). The reference categories used were: no current depressive symptoms (RQ1), no depressive symptoms at both time points

**Table 1**  
Scoring criteria of the Mediterranean Diet Score, Alternative Healthy Eating Index 2010 and Dietary Approaches to Stop Hypertension score used in the Longitudinal Aging Study Amsterdam.

Mediterranean diet score Component	Criterion for score 0	Criterion for score 1	Criterion for score 2	Criterion for score 3	Criterion for score 4	Criterion for score 5	Alternative healthy eating index 2010 <sup>a</sup> Component	Criterion for minimum score (0)	Criterion for maximum score (10)	Dietary approaches to stop hypertension score <sup>b</sup> Component	Criterion for minimum score (0)	Criterion for maximum score (5)
Fruits	0 serv/wk	< 5 serv/wk	5–9 serv/wk	9–16 serv/wk	16–22 serv/wk	≥ 22 serv/wk	Fruit	0 serv/d	≥ 4 serv/d	Fruits and fruit juices	quintile 1	quintile 5
Vegetables	0 serv/wk	< 7 serv/wk	7–13 serv/wk	13–21 serv/wk	21–33 serv/wk	≥ 33 serv/wk	Vegetables	0 serv/d	≥ 5 serv/d	Vegetables	quintile 1	quintile 5
Legumes	0 serv/wk	< 1 serv/wk	1–3 serv/wk	3–5 serv/wk	5–6 serv/wk	≥ 6 serv/wk	Nuts and legumes	0 serv/d	≥ 1 serv/d	Nuts and legumes	quintile 1	quintile 5
Potatoes	0 serv/wk	< 5 serv/wk	5–9 serv/wk	9–13 serv/wk	13–18 serv/wk	≥ 18 serv/wk						
Non-refined cereals	0 serv/wk	< 7 serv/wk	7–13 serv/wk	13–19 serv/wk	19–32 serv/wk	≥ 32 serv/wk	Whole grains	0 g/d (men)	6 serv/d (men)	Whole grains	quintile 1	quintile 5
Red meat and products <sup>c</sup>	> 10 serv/wk	8–10 serv/wk	6–8 serv/wk	4–6 serv/wk	1–4 serv/wk	≤ 1 serv/wk	Red/processed meat <sup>c</sup>	0 g/d (women)	5 serv/d (women)	Red and processed meats <sup>c</sup>	quintile 5	quintile 1
Poultry <sup>c</sup>	> 10 serv/wk	9–10 serv/wk	7–9 serv/wk	5–7 serv/wk	3–5 serv/wk	≤ 3 serv/wk						
Fish	0 serv/wk	< 1 serv/wk	1–3 serv/wk	3–5 serv/wk	5–6 serv/wk	≥ 6 serv/wk	EPA + DHA	0 mg/d	≥ 250 mg/d			
Olive oil (1 serving = 15 ml)	0 serv/wk	< 0.5 serv/wk	0.5–1 serv/wk	1–3 serv/wk	3–7 serv/wk	> 7 serv/wk	Polyunsaturated fatty acids	≤ 2 E%	≥ 10 E%			
Full-fat dairy products <sup>c</sup>	> 30 serv/wk	29–30 serv/wk	21–29 serv/wk	16–21 serv/wk	11–16 serv/wk	≤ 11 serv/wk	Trans fat <sup>c</sup>	≥ 4 E%	≤ 0.5 E%	Low-fat dairy	quintile 1	quintile 5
Alcoholic beverages <sup>c</sup> (1 serving = 1 glass containing 12 g ethanol)	> 7 or 0 serv/d	6–7 serv/d	5–6 serv/d	4–5 serv/d	3–4 serv/d	< 3 serv/d	Sugar-sweetened beverages and fruit juice <sup>c</sup>	≥ 1 drink/d	0 drinks/d	Sweetened beverages <sup>c</sup>	quintile 5	quintile 1
							Alcoholic drinks <sup>c</sup>	≥ 3.5 drinks/d (men)	0–2.0 drinks/d (men)			
								≥ 2.5 drinks/d (women)	0–1.5 drinks/d (women)			
<b>Total score</b>	<b>0</b>					<b>55</b>	<b>Total score</b>	<b>0</b>	<b>100</b>	<b>Total score</b>	<b>0</b>	<b>35</b>

Abbreviations: DHA, docosahexaenoic acid; E%, energy percent; EPA, eicosapentaenoic acid; serv, serving.

<sup>a</sup> For the AHEI-2010, scores 1 to 9 correspond to intakes that proportionally lie between the given intakes of the scores 0 and 10.

<sup>b</sup> The DASH intake quintiles are in g/d.

<sup>c</sup> For this component, the scoring is reverse (i.e. high intake = low score).



(RQ2) and no history of depressive symptoms (RQ3). Effect-modification by sex, age (continuous) and cohort was tested for all RQs as diet-depression associations have been found to be sex- and age-specific (Akbaraly et al., 2013; Gougeon, 2016) and as the LASA's cohorts differ in age range and assessment period. The potential effect-modifier and the interaction term between the depression determinant and the potential effect-modifier were included in the crude regression models, and a  $P$ -value  $< 0.10$  of an interaction term was considered statistically significant. Potential confounders were added to the univariable models of the cross-sectional analyses (RQ1), and included in the final models if regression coefficients changed  $> 10\%$  for at least one of the diet indices. This led to the following models used for RQ1, RQ2 and RQ3: model 1 was the crude model, model 2 was adjusted for age, sex, cohort, education level and marital status, and model 3 was additionally adjusted for physical activity, smoking and number of chronic diseases. Energy intake as well as waist circumference were additionally added to the models to examine the influence of these variables separately. For RQ3, model 3 was also adjusted for current depressive symptoms (at the side study, continuous) to investigate the associations independently of one's mood status at the time of the FFQ. For completeness, this additional adjustment was also done for RQ2; however, current depressive symptoms (2014/2015) were measured before the second CES-D measurement of the change (2015/2016; see Fig. 1).

To test the robustness of our findings, several sensitivity analyses were conducted. As alcohol is one of the components of the MDS and AHEI but not the DASH, all analyses with the DASH were additionally adjusted for alcohol use. Further, the regression analyses were repeated after the exclusion of participants with an MMSE score  $< 24$  at the regular cycle just before (2011–2013) and/or after (2015/2016) the side study (RQ1+2+3) to avoid any bias regarding dietary recall caused by cognitive impairment. Analyses were also repeated after excluding participants using antidepressants at the cycles the CES-D data were used for each RQ.

Two-sided  $P$ -values  $\leq 0.05$  were considered statistically significant. SPSS version 24 (SPSS Inc. Chicago, IL, USA) was used for all analyses.

### 3. Results

#### 3.1. Characteristics

Table 2 shows the characteristics of the three samples. The 1322 participants of the cross-sectional sample (51.9% women) had a median age of 65.1 years (IQR: 61.1–72.0) at the cycle before the side study (2011–2013). The median age of the change sample ( $n = 1233$ , 51.5% women) was 65.2 years (IQR: 61.2–71.9) and of the history sample ( $n = 687$ , 50.5% women) 71.2 years (IQR: 67.2–77.2). Compared to the cross-sectional and change samples, the history sample was lower educated, had a lower energy intake and had more chronic diseases.

#### 3.2. Depressive symptoms

For the cross-sectional sample, the median CES-D score was 8.0 (IQR: 4.0–13.0) (Table 2). Regarding the change sample, clinically relevant depressive symptoms (CES-D  $\geq 16$ ) were experienced by 120 participants (9.7%) in 2011–2013 and by 130 participants (10.5%) in 2015/2016. The majority (84.8%) had no depressive symptoms at both cycles, while 5.4% experienced emerging, 4.6% remitted and 5.1% chronic/recurrent depressive symptoms (Table 2). For the history sample, the numbers of depressive symptoms were 69 (10.0%), 67 (9.8%), 59 (8.6%) and 60 (8.7%) at the four regular cycles from 2001–2003 to 2011–2013. In total 144 participants (21.0%) had a history of depressive symptoms (ever CES-D  $\geq 16$  from 2001–2003 to 2011–2013) (Table 2), of which 20 had a CES-D  $\geq 16$  only in 2011–2013.

#### 3.3. Dietary intake

In Supplemental Table 1, median intakes of the components of the *a priori* indices are shown for the three analytical samples. Compared to the intakes of the cross-sectional and change samples, the intakes of vegetables, nuts and olive oil of the history sample were lower, whereas intakes of potatoes and full-fat dairy were higher.

##### 3.3.1. RQ1: cross-sectional analyses

Interaction terms between the presence of depressive symptoms and age or cohort were not significant, but those with sex were significant for two indices (MDS:  $P = 0.133$ , AHEI:  $P = 0.004$ , DASH:  $P = 0.022$ ). To be able to compare the indices, all analyses were stratified by sex (Table 3). In crude models, depressive symptoms were cross-sectionally associated with lower MDS scores; however, after adjustment for confounders, the association remained only statistically significant in men (B model 3:  $-1.21$ , 95% CI:  $-2.41$ ,  $-0.023$ ). Current depressive symptoms were also associated with a lower AHEI score in men (B model 3:  $-2.72$ , 95% CI:  $-5.24$ ,  $-0.20$ ) but not in women. An unexpected positive association with the DASH score in women became apparent in model 3 (B:  $0.86$ , 95% CI:  $0.072$ ,  $1.66$ ). Additional adjustment for energy intake and waist circumference did not change the findings of any diet index.

##### 3.3.2. RQ2: change analyses

Table 4 shows the results of the association between short-term changes in depressive symptoms and the diet indices. The emerging, remitted and chronic/recurrent groups were associated with lower scores on all diet indices; however, these associations were not all significant. After adjustment for confounders, participants with chronic/recurrent depressive symptoms had a lower MDS score compared to those with no depressive symptoms (B model 3:  $-2.22$ , 95% CI:  $-3.40$ ,  $-1.04$ ). This inverse association was also shown for the AHEI score, although the association was attenuated in model 3 (B:  $-2.37$ , 95% CI:  $-4.92$ ,  $0.18$ ). No significant associations were found for the DASH score. The additional inclusion of energy intake and waist circumference in the models did not change the findings of any diet index. Of the 63 participants with chronic/recurrent depressive symptoms, 47 had current depressive symptoms at the time of the FFQ. However, additional adjustment for current depressive symptoms did not change the findings (MDS: B:  $-1.93$ , 95% CI:  $-3.23$ ,  $-0.62$ ; AHEI: B:  $-2.29$ , 95% CI:  $-5.11$ ,  $0.53$ ).

Only for the MDS, a significant interaction term was found with sex (remitted group:  $P = 0.085$ ). After stratification by sex, the association of the chronic/recurrent group with the MDS score was only significant for women (B:  $-2.71$ , 95% CI:  $-4.02$ ,  $-1.30$ ) but not for men in model 3. In addition, significant interaction terms were found between some of the change-groups and cohorts ( $P < 0.09$ ) for all diet indices; stratification by cohort showed associations between the chronic/recurrent group and the MDS score only in cohort 2 (B model 3:  $-2.04$ , 95% CI:  $-4.10$ ,  $0.006$ ) and cohort 3 (B model 3:  $-2.46$ , 95% CI:  $-4.19$ ,  $-0.74$ ), but not in cohort 1, and no associations for the AHEI and DASH in any of the cohorts. Because of the small number of men ( $n = 16$ ) and of cohort 1 ( $n = 14$ ) in the chronic/recurrent group in the stratified analyses, the reliability of these stratified results is uncertain. Unstratified results are presented (Table 4) as interactions were not consistent for all indices.

##### 3.3.3. RQ3: history analyses

Of the 144 participants with a history of depressive symptoms, 68 (47%) had current depressive symptoms. Interaction terms between history of depressive symptoms and age or cohort were not significant, but those with sex were significant for the AHEI and DASH (MDS:  $P = 0.114$ , AHEI:  $P = 0.001$ , DASH:  $P = 0.010$ ). After stratification of all indices by sex, men with a long-term history of depressive symptoms scored lower on the MDS (B model 4:  $-1.87$ , 95% CI:  $-3.47$ ,  $-0.27$ )

**Table 2**  
Characteristics of the samples of middle-aged and older adults used for the three research questions in the Longitudinal Aging Study Amsterdam<sup>a</sup>.

	<i>n</i>	Cross-sectional sample (RQ1) 1312	Change sample (RQ2) 1233	History sample (RQ3) 687
Age (years)		65.1 [61.1–72.0]	65.2 [61.2–71.9]	71.2 [67.2–77.2]
Sex, <i>n</i> (%) female		681 (51.9)	635 (51.5)	347 (50.5)
Cohort				
	<i>First</i>	252 (19.2)	230 (18.7)	241 (35.1)
	<i>Second</i>	456 (34.8)	444 (36.0)	446 (64.9)
	<i>Third</i>	604 (46.0)	559 (45.3)	–
Education, <i>n</i> (%)				
	<i>Low</i>	159 (12.1)	143 (11.6)	111 (16.2)
	<i>Middle</i>	769 (58.6)	719 (58.3)	403 (58.7)
	<i>High</i>	384 (29.3)	371 (30.1)	173 (25.2)
Marital status, <i>n</i> (%)				
	<i>Married</i>	948 (72.3)	894 (72.5)	472 (68.7)
	<i>Never married</i>	101 (7.7)	96 (7.8)	38 (5.5)
	<i>Widowed/divorced</i>	263 (20.0)	243 (19.7)	177 (25.8)
Body mass index (kg/m <sup>2</sup> )		26.8 [24.3–29.6]	26.8 [24.3–29.5]	27.0 [24.7–29.6]
Waist circumference (cm)		97.8 ± 11.9	97.8 ± 12.0	98.9 ± 10.7
Physical activity (MET h/wk)		53.4 [33.0–79.3]	53.5 [33.6–79.1]	51.9 [33.8–76.8]
Smoking, <i>n</i> (%)				
	<i>Never</i>	364 (27.7)	336 (27.3)	192 (27.9)
	<i>Former</i>	792 (60.4)	751 (60.9)	426 (62.0)
	<i>Current</i>	156 (11.9)	146 (11.8)	69 (10.0)
Alcohol use, <i>n</i> (%)				
	<i>Non-drinker</i>	161 (12.3)	143 (11.6)	87 (12.7)
	<i>Light</i>	620 (47.3)	581 (47.1)	354 (51.5)
	<i>Moderate</i>	454 (34.6)	434 (35.2)	214 (31.1)
	<i>(Very) excessive</i>	77 (5.9)	75 (6.1)	32 (4.7)
Energy intake (kCal/d)		2089 ± 574	2094 ± 574	2059 ± 562
Number of chronic diseases, <i>n</i> (%)				
	<i>0 chronic disease</i>	207 (15.8)	198 (16.1)	68 (9.9)
	<i>1 chronic disease</i>	369 (28.1)	345 (28.0)	180 (26.2)
	<i>≥ 2 chronic diseases</i>	736 (56.1)	690 (56.0)	439 (63.9)
Cognitive functioning (MMSE score)		29 [28–30]	29 [28–30]	29 [28–30]
Use of antidepressants, <i>n</i> (%)		71 (5.4)	66 (5.4)	26 (3.8)
Depressive symptoms (CES-D score)		8.0 [4.0–13.0]	8.0 [4.0–13.0]	9.0 [5.0–14.0]
Presence of depressive symptoms (CES-D score ≥ 16), <i>n</i> (%)		208 (15.9)	194 (15.7)	119 (17.3)
Short-term changes in depressive symptoms, <i>n</i> (%)				
	<i>No</i>	–	1046 (84.8)	–
	<i>Emerging</i>	–	67 (5.4)	–
	<i>Remitted</i>	–	57 (4.6)	–
	<i>Chronic/recurrent</i>	–	63 (5.1)	–
Long-term history depressive symptoms, <i>n</i> (%)		–	–	144 (21.0)
Mediterranean Diet Score		32.6 ± 4.8	32.7 ± 4.8	32.3 ± 4.8
Alternative Healthy Eating Index 2010		58.4 ± 10.2	58.6 ± 10.2	57.8 ± 9.7
Dietary Approaches to Stop Hypertension score		21.6 ± 4.4	21.6 ± 4.4	21.3 ± 4.2

Abbreviations: CES-D, Center for Epidemiologic Studies Depression scale; MET, Metabolic Equivalent of Task; RQ, research question; SD, standard deviation. Values are displayed as mean ± SD or median [interquartile range], and as *n* (%).

<sup>a</sup> Characteristics are measured in 2011–2013, except for energy intake, use of antidepressants, (presence of) depressive symptoms, and the diet quality indices, which are measured at the Nutrition and Food-related Behaviour study (2014/2015).

**Table 3**  
Cross-sectional associations between depressive symptoms and three diet quality indices stratified by sex in 1312 middle-aged and older LASA participants<sup>a</sup>.

		MDS				AHEI				DASH			
		B	95% CI		<i>P</i>	B	95% CI		<i>P</i>	B	95% CI		<i>P</i>
Model 1	Male	–2.09	–3.31	–0.88	0.001	–4.48	–7.04	–1.93	0.001	–0.96	–2.09	0.18	0.098
	Female	–0.93	–1.83	–0.03	0.043	0.19	–1.71	2.09	0.845	0.65	–0.14	1.45	0.108
Model 2	Male	–1.52	–2.72	–0.32	0.013	–3.40	–5.93	–0.88	0.008	–0.64	–1.77	0.49	0.270
	Female	–0.67	–1.56	0.21	0.136	0.88	–1.01	2.77	0.359	0.74	–0.05	1.54	0.066
Model 3	Male	–1.21	–2.41	–0.02	0.046	–2.72	–5.24	–0.20	0.034	–0.40	–1.53	0.73	0.492
	Female	–0.50	–1.38	0.38	0.264	1.20	–0.70	3.10	0.215	0.86	0.07	1.66	0.033

Abbreviations: AHEI, Alternative Healthy Eating Index 2010; B, unstandardised regression coefficient; CES-D, Center for Epidemiologic Studies Depression scale; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; LASA, Longitudinal Aging Study Amsterdam; MDS, Mediterranean Diet Score.

Model 1: crude model.

Model 2: adjusted for age, cohort, education level and marital status.

Model 3: additionally adjusted for physical activity, smoking and number of chronic diseases.

<sup>a</sup> Clinically relevant depressive symptoms were defined as a CES-D score ≥ 16. Number of cases: men: 65 / 631; women: 143 / 681.

**Table 4**Associations between short-term changes in depressive symptoms and three diet quality indices in 1233 middle-aged and older LASA participants<sup>a</sup>.

		MDS				AHEI				DASH			
		B	95% CI		P	B	95% CI		P	B	95% CI		P
Model 1	No	Reference				Reference				Reference			
	Emerging	–1.32	–2.49	–0.14	0.028	–0.99	–3.51	1.53	0.441	–0.32	–1.41	0.76	0.556
	Remitted	–1.10	–2.37	0.17	0.090	–1.16	–3.88	1.56	0.402	–0.40	–1.57	0.77	0.499
	Chronic/recurrent	–3.24	–4.45	–2.03	< 0.001	–3.78	–6.38	–1.19	0.004	–0.63	–1.75	0.48	0.263
Model 2	No	Reference				Reference				Reference			
	Emerging	–0.92	–2.08	0.23	0.116	–0.57	–3.04	1.91	0.653	–0.45	–1.52	0.61	0.403
	Remitted	–0.70	–1.94	0.54	0.268	–0.73	–3.38	1.93	0.592	–0.36	–1.50	0.78	0.531
	Chronic/recurrent	–2.58	–3.77	–1.38	< 0.001	–3.02	–5.58	–0.46	0.021	–0.66	–1.76	0.44	0.241
Model 3	No	Reference				Reference				Reference			
	Emerging	–0.72	–1.85	0.42	0.215	–0.15	–2.59	2.30	0.905	–0.33	–1.38	0.72	0.532
	Remitted	–0.33	–1.55	0.89	0.596	0.08	–2.56	2.71	0.955	–0.06	–1.19	1.07	0.914
	Chronic/recurrent	–2.22	–3.40	–1.04	< 0.001	–2.37	–4.92	0.18	0.069	–0.43	–1.52	0.67	0.445

Abbreviations: AHEI, Alternative Healthy Eating Index 2010; B, unstandardised regression coefficient; CES-D, Center for Epidemiologic Studies Depression scale; CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; LASA, Longitudinal Aging Study Amsterdam; MDS, Mediterranean Diet Score.

Model 1: crude model.

Model 2: adjusted for age, sex, cohort, education level and marital status.

Model 3: additionally adjusted for physical activity, smoking and number of chronic diseases.

<sup>a</sup> Changes in depressive symptoms were divided into four categories, based on the presence of depressive symptoms (CES-D score  $\geq 16$ ) in 2011–2013 and 2015/2016.**Table 5**Associations between long-term history of depressive symptoms and three diet quality indices stratified by sex in 687 middle-aged and older LASA participants<sup>a</sup>.

		MDS				AHEI				DASH			
		B	95% CI		P	B	95% CI		P	B	95% CI		P
Model 1	Male	–2.10	–3.53	–0.67	0.004	–4.52	–7.41	–1.63	0.002	–1.15	–2.48	0.17	0.088
	Female	–0.62	–1.75	0.51	0.279	1.73	–0.59	4.05	0.144	0.97	0.01	1.92	0.048
Model 2	Male	–2.00	–3.44	–0.56	0.007	–4.92	–7.85	–1.99	0.001	–1.33	–2.70	0.04	0.057
	Female	–0.14	–1.28	1.00	0.812	2.71	0.34	5.08	0.025	1.11	0.13	2.10	0.027
Model 3	Male	–1.88	–3.33	–0.42	0.012	–4.56	–7.47	–1.64	0.002	–1.17	–2.54	0.21	0.096
	Female	–0.31	–1.45	0.82	0.588	2.53	0.13	4.92	0.039	0.95	–0.03	1.93	0.056
Model 4	Male	–1.87	–3.47	–0.27	0.022	–4.33	–7.54	–1.13	0.008	–1.12	–2.63	0.40	0.148
	Female	0.11	–1.20	1.42	0.867	2.06	–0.71	4.82	0.144	0.86	–0.27	1.99	0.133

Abbreviations: B, unstandardised regression coefficient; CES-D, Center for Epidemiologic Studies Depression scale; CI, confidence interval; LASA, Longitudinal Aging Study Amsterdam.

Model 1: crude model.

Model 2: adjusted for age, cohort, education level and marital status.

Model 3: additionally adjusted for physical activity, smoking and number of chronic diseases.

Model 4: additionally adjusted for current depressive symptoms (continuous, at side study).

<sup>a</sup> History of depressive symptoms was defined as a CES-D score ever  $\geq 16$  from 2001–2003 to 2011/2012. Number of cases: men: 37 / 340; women: 82 / 347.

as well as on the AHEI (B model 4: –4.33, 95% CI: –7.54, –1.13), independent of current depressive symptoms (Table 5). In women, a history of depressive symptoms was not associated with the MDS, but with higher AHEI and DASH scores in two models; however, after adjustment for current depressive symptoms (model 4), these associations were no longer statistically significant. Additional adjustment for energy intake and waist circumference did not change the findings.

### 3.4. Sensitivity analyses

Additional adjustment for the use of alcohol for the DASH did not result in different findings for any of the three RQs. Similarly, exclusion of participants with an MMSE score < 24 in 2011–2013 and/or in 2015/2016 (RQ1:  $n = 45$ ; RQ2:  $n = 44$ ; RQ3:  $n = 29$ ) did not change the results of any RQ for any diet index. After exclusion of participants who used antidepressants at the indicated cycles (RQ1:  $n = 71$ ; RQ2:  $n = 100$ ; RQ3:  $n = 64$ ), the cross-sectional associations became non-

significant in men for the MDS (B model 3: –0.92, 95% CI: –2.18, 0.34) and the AHEI (B model 3: –2.18, 95% CI: –4.85, 0.50), and in women for the DASH (B model 3: 0.66, 95% CI: –0.18, 1.50). The changes and history associations did not change, except that the association between history and the MDS in men attenuated (B model 4: –1.72, 95% CI: –3.50, 0.07).

## 4. Discussion

In Dutch middle-aged and older adults, current and past depressive symptoms were associated with poorer diet quality based on indices. Depressive symptoms were cross-sectionally associated with lower MDS and AHEI scores in men, but not in women. Chronic/recurrent depressive symptoms over 2 to 5 years were associated with lower MDS and AHEI scores, while emerging and remitted depressive symptoms were not associated with any of the diet indices. A history of depressive symptoms over 2 to 14 years was associated with lower MDS and AHEI



scores in men. No consistent associations with the DASH score were found.

We found associations with a lower diet quality in men not only cross-sectionally for the presence of current depressive symptoms, but also longitudinally for history of depressive symptoms in both the short- and long-term. Hence, having a depressed mood currently or previously seems to be associated with a less healthy dietary pattern in men. However, the cross-sectional MDS and AHEI associations became non-significant when persons using antidepressants were excluded. This might indicate that these associations are partly driven by men with more severe depressive symptoms (who used antidepressants); yet, the regression coefficients did not differ that much (MDS:  $-1.21$  (complete sample) vs.  $-0.92$  (without antidepressant users); AHEI:  $-2.72$  vs.  $-2.18$ ). Regarding the short-term changes in depressive symptoms, we only found an association for the chronic/recurrent group. This indicates that chronically/recurrently depressed persons consume a less healthy diet, but that emerging or remitted depression does not seem to negatively influence diet.

Next, we found that some associations differed between men and women. The current and long-term history associations were comparable in direction and effect size, showing inverse associations with the MDS and AHEI in men but not in women. Reasons for these sex differences are not clear, but it might be that depressive mood negatively influences food intake to a greater extent in men than in women. In contrast, women who have/had depressive symptoms might pay more attention to their food intake, resulting in 'normal' MDS and AHEI scores and, consequently, no associations. In cancer patients, changes towards a healthier diet were significantly more frequent in women compared to men (Gavazzi et al., 2018). The associations of chronic/recurrent depressive symptoms with the MDS and AHEI were found in both sexes; though, when the MDS analysis was stratified, the association was only found in women. A potential explanation for this null-association in men is the low power (16 men with chronic/recurrent depressive symptoms). Lastly, our sex differences might also be explained by chance.

Our findings also showed that the associations of the three RQs were comparable for the MDS and the AHEI: current as well as past depressive symptoms were associated with lower index scores in men. In contrast, we did not find any associations between the depression determinants and the DASH, except for a higher DASH score in women with current depressive symptoms (only model 3). This unexpected direction – depressive symptoms may lead to a healthier diet – was also seen in women for the AHEI but only for the DASH significant. The null-findings for the DASH might be explained by its relatively smaller number of components and smaller score range, compared to the other indices. In contrast to the MDS, which includes fish and olive oil, and the AHEI, which includes eicosapentaenoic/docosahexaenoic acid and polyunsaturated fatty acids, the DASH does not include any fish or fatty acid component. The DASH also does not take into account alcoholic beverages. These food groups might be key components in the depression-diet link (Grosso et al., 2016; Kyrozi et al., 2009). Another explanation may be the inclusion of fruit juices in the fruit component, i.e. scoring them as healthy. In the AHEI, fruit juices are scored as unhealthy, together with sugar-sweetened beverages. A final possible explanation is the healthy-scoring low-fat dairy component: this component was not included in the MDS or AHEI and may have influenced the total DASH score in such a way that associations were attenuated.

This study is the first that addressed the reverse causality hypothesis by investigating depressive symptoms prospectively in relation to three diet quality indices. Our findings are somewhat different from previous studies. Gougeon et al. (2017) studied the hypothesis in an older sample, like us. They found no different changes in intakes of energy, fibre, protein and saturated fat between persons who became depressed and those who remained non-depressed. However, a comparison with our study is hard, since their follow-up time was short (1 year), they did not examine diet indices, and their design did not eliminate the

possibility of studying the reverse association (i.e. 1-year change in intake  $\rightarrow$  incident depressive symptoms in that year) because it was unknown in which month the changes in intake and mood occurred. Our study compares better to the Australian study of Jacka et al. (2015) in that they studied dietary patterns as well as current and past depression. Similar to our cross-sectional MDS and AHEI associations in men, they found that current depression was associated with lower scores on their healthy pattern (no sex-stratified analyses). However, those with a depression history reported higher scores on the healthy pattern (if they had received treatment) and lower scores on the unhealthy pattern. This contrasts with our significant associations between long-term history of depressive symptoms and lower MDS and AHEI scores in men. Adjustment for current depressive symptoms was done in both studies, so could not explain these differences. Explanations could be age differences between the study populations and Jacka's reliance on retrospectively recalled depression with no specified time frame, while we used prospective CES-D data from four regular interviews over 2 to 14 years.

Our findings that depressive symptoms were associated with lower diet quality are contrary to additional analyses of some prospective studies on the diet-depression link. None of these studies that additionally analysed the association in the reverse direction or excluded participants reporting depressive symptoms at baseline from the analysis, found evidence for reverse causality (e.g. Akbaraly et al., 2009; 2013; Chocano-Bedoya et al., 2013; Kingsbury et al., 2016; Knüppel et al., 2017; Rienks et al., 2013; Sánchez-Villegas et al., 2009; Skarupski et al., 2013; Smith et al., 2014; Tsai et al., 2012). An important difference with our study is that most of them did not examine *a priori* diet indices, but *a posteriori* patterns (Akbaraly et al., 2009; Chocano-Bedoya et al., 2013; Rienks et al., 2013) or food groups (Kingsbury et al., 2016; Knüppel et al., 2017; Smith et al., 2014; Tsai et al., 2012). Akbaraly et al. (2013) and Sánchez-Villegas et al. (2009) used, respectively, the AHEI and MDS, yet older versions. Similar to us, Skarupski et al. (2013) used the MDS of Panagiotakos et al. (2007) but they just excluded participants with depressive symptoms at baseline and did no analysis with the CES-D as determinant. Moreover, our cross-sectional associations were not significant in women. Some previous cross-sectional studies on diet quality (i.e. AHEI) were performed only in women; they showed that depressive symptoms were associated with a lower AHEI score in depressed, obese women (Appelhans et al., 2012) and in Latinos at risk of type 2 diabetes (Pagoto et al., 2009), but not in overweight African American women (Whitaker et al., 2014). Additionally, current depressive disorder was associated with lower MDS and AHEI scores (Gibson-Smith et al., 2018). Potential explanations for these inconsistencies are differences in study populations, measures of depression and dietary assessment methods.

Strengths of our study include the large, nationally representative sample of Dutch middle-aged and older adults, its longitudinal design, the use of three depression determinants across different time windows (current, short-term changes and long-term history), and the use of three commonly-used indices of a healthy diet. Some limitations of the study should also be discussed. Dietary data from an FFQ were used for the outcome measures of this study; potential memory loss in older participants might have led to misreporting (McNeill et al., 2009). Nonetheless, underreporting in older persons may partly reflect a true low caloric intake (undereating) (Shahar et al., 2010), and exclusion of participants with low cognitive functioning did not change the results. Another caveat is that the FFQ data were collected as part of the study (2014/2015) and not at a regular cycle; this resulted in time differences with the cycles of the covariates (2011–2013) and the second CES-D measurement of RQ2 (2015/2016). Potential changes in lifestyle (diet, physical activity, smoking, alcohol use) within these time difference periods could have introduced information bias. Since dietary data were only collected once, it was not possible to investigate the prospective depression-diet association in order to completely test the reverse causality hypothesis within LASA. Moreover, our study was

limited by the use of the CES-D scale, which assesses self-reported depressive symptoms but not clinical major depressive disorder. Also, its mode at the side study (questionnaire) differed from the one at regular cycles (face-to-face interview). Finally, as participation in the side study was the main inclusion criteria, our sample might be relatively healthy and less representative.

In conclusion, our longitudinal study in middle-aged and older adults shows that current depressive symptoms, short-term chronic/recurrent depressive symptoms and a long-term history of depressive symptoms were all associated with lower diet quality scores, indicating a less healthy diet. These associations were found for adherence to the MDS and AHEI and were particularly present among men. Depressive symptoms did not seem to be associated with the DASH. This all gives an indication of reversed causality of diet and depression, while emphasising potential sex differences. As longitudinal studies on the depression to diet association are scarce, more prospective studies are needed to confirm our results. Such studies should preferably include repeated diet measurements and investigate gender differences. If future studies find more evidence for an association between low mood and poor diet (in men), clinicians and practitioners need to be aware of this in order to prevent this undesirable change in diet and subsequent increased disease risk.

### Authors' contributions

LEME, IAB and MV designed the study. LEME and LHHW collected the data. LEME performed the statistical analyses and wrote the first draft of the paper with contributions from LHHW, BWJHP, IAB and MV. LEME had primary responsibility for final content. All authors read and approved the final manuscript.

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### Conflicts of interest

None

### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jad.2019.02.004](https://doi.org/10.1016/j.jad.2019.02.004).

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